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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/987,931	11/16/2001	Kevin Qun Fang	4821-439-999	7960

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EXAMINER	
KIM, VICKIE Y	

ART UNIT	PAPER NUMBER
1614	8

DATE MAILED: 09/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/987,931	Applicant(s) FANG ET AL.	
	Examiner Vickie Kim	Art Unit 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7 and 19-126* is/are pending in the application.

4a) Of the above claim(s) *1-7, 29-126* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3&4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election acknowledged

1. Applicants affirmation on the election with traverse of Group II, claims 19-28 is acknowledged. Applicant's traverse the restriction requirement on the grounds that there would be no burden in searching the entire application. This argument is not persuasive, as not all groups encompassed by the application would be classified together. As mentioned in previous office action, each invention is found to be patentably distinct subject matter proven in numerous patent literatures. For instance, US6197827 is directed to a treatment of specific condition such as nicotine addiction using antidepressant such as bupropion. Additionally, since each invention contains materially different disorder caused by different etiologies and involve different pathologies, the treatment can be achieved by materially different product. As evidenced by numerous documents, it is clear that each invention is patentably distinct and therefore, the search is burdensome. Furthermore, even if there were unity of classification, the search of the entire application in patent and non-patent literature (a significant part of the thorough examination) would be burdensome due to the reasons mentioned in previous office action(e.g. patentably distinct subject matter proven in numerous patent literature). Therefore the restriction requirement is maintained and made FINAL.

Status of Application

2. The claims 1-7, 19-126 are pending, and the elected claims 19-28 are presented for the examination. The non-elected claims 1-7 and 29-126 are withdrawn from the consideration.

Information Disclosure Statement

3. Applicant's information disclosure statements received 02/15/2002 and 06/24/2002 have been considered. Please refer to Applicant's copy of the 1449 submitted herewith.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

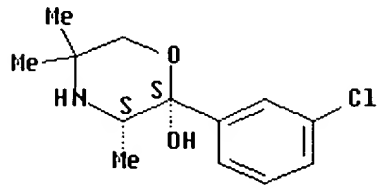
> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

2. Claims 19-23, 26 and 28 are rejected under 35 U.S.C. 102(a) as being anticipated by Morgan et al (WO99/37305).

The claims are drawn to a method of treating an affective disorders(e.g. depression or nicotine addiction) using an effective amount of a bupropion metabolite such as optically pure (S,S)-hydroxybupropion.

WO'305 teaches a morpholinol compound (e.g. (+)-(2S, 3S)-2-(3-chlorophenyl)-3,5,5-trimethyl-2-morpholinol) that is an active metabolite of bupropion and its use in the treatment of depression or nicotine addiction, see abstract, claims and column 2, lines 1-14. Especially, WO'305 teaches optically pure (S,S)-hydroxybupropion that is formed from hydroxylation(i.e. 2-hydroxy) of the tert-butyl group of bupropion, see column 2, thru column 4, lines 3.

AS to claims 21-22, for instance, most active optically pure metabolite compound(e.g. (+)-(2S, 3S)-2-(3-chlorophenyl)-3,5,5-trimethyl-2-morpholinol(same as (S,S)-2-(3-chlorophenyl)-2-hydroxy-3,5,5-trimethyl-2-morphinol) or its hydrochloride salt, see claims 1-2) of the formula I found in the cited patent has a structure as following:



As to the claim 23, WO305 teaches that the patented compound of formula I(i.e.(+)-(2S, 3S)-2-(3-chlorophenyl)-3,5,5-trimethyl-2-morpholinol) does not show the toxic effect that is associated with other metabolites, see page 11, lines 4-5 and pages 13-14 .

Thus, all the critical elements required by the instant claims are taught by the cited reference and all the claims 19-23, 26 and 28 are anticipated by the prior art of the record.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 24-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morgan et al (WO99/37305) in view of Cary(WO99/17803).

Morgan's teaching is mentioned immediately above in 102 rejection.

Applicants claim differs because it requires combination drug therapy with secondary active agent.

However it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify WO'305 to add secondary active agent to improve the therapeutic efficacy when WO'305 is taken in view of WO'803 because WO'803 teaches a combination drug therapy to treat nicotine addiction. WO'803 teaches a method of treating nicotine addiction using an antidepressant(e.g.bupropion) alone or in combination with nicotine transdermal patch, see page 8, lines 1-5. Additionally , it is also conventional knowledge that the combination drug therapy beneficially lowers the dose of active agent used in the treatment because each agent utilizes different underlying mechanism.

Thus, one would have motivated to do so to maximize the therapeutic efficacy by lowering the dose required and reduces the toxic side effect that is often associated with high therapeutic dose as suggested in WO'803.

3. Claim 27 is rejected under 35 U.S.C. 103(a) as being unpatentable over Mccullough et al(WO99/38499) in view of Morgan et al (WO99/37305).

WO'499 teaches a method of treating an affective disorder such as depression, or narcolepsy using an effective amount of bupropion, see abstract and page 2, lines 24-34.

Applicants claim differs because it require active metabolite such as (S,S)-hydroxybupropion.

However, at the time of the invention was made, it would have been obvious to one of ordinary skill in the art to extend WO'499 teaching to include a metabolite of bupropion such as hydroxybupropion(i.e. (+)-(2S, 3S)-2-(3-chlorophenyl)-3,5,5-trimethyl-2-morpholinol) into the list of therapeutic modalities to treat affective disorders when WO'499 is taken in view of WO' 305 because WO'305 teaches that hydroxybupropion(i.e. (+)-(2S, 3S)-2-(3-chlorophenyl)-3,5,5-

trimethyl-2-morpholinol) is an active metabolite of bupropion that is effective in treating all the disorders that is treated by bupropion. Since bupropion is effective in the treatment of narcolepsy, the active metabolite is deems to be effective in the treatment of narcolepsy. This allegation is supported by the statement found in WO'305 where both bupropion and the active metabolite utilizes the very same biological pathway (i.e. noradrenergic(NA) mechanism) that is responsible for the treatment of affective disorders such as depression or nicotine addictive, see page 12 of WO'305. Since depression or nicotine addiction is the functional equivalent to narcolepsy as evidenced by applicabt's own admission (see the instant specification at page 7, lines 7-11), all the species of affective disorders are effectively treated by not only bupropion but also the active metabolite of bupropion as well. Thus, it would have been obvious to one of ordinary skill in the art to apply active metabolite to treat narcolepsy with reasonable expectation of success.

For instance, WO'499 teaches that the behavioral and electrophysiological data suggest that the affective disorders such as depression or nicotine addiction utilizes noradrenergic(NA) mechanism as well as effects of bupropion(wellbutrin®) mediated by a noradrenergic(NA) mechanism where the said morpholinol metabolite of bupropion has shown stronger therapeutic effectiveness due to twice as potent as bupropion(Wellbutrin®) as an NA inhibitor. Furthermore, WO'305 also teaches that the active metabolite do not show toxic side effect within the therapeutic dosage range, see page 11, lines 4-5 and pages 13-14.

Thus, one would have been motivated to so because it is always desired to have more number of the therapeutic modalities, especially when the substitution provides improved quality

of the treatment so that patients achieve optimal therapeutic efficacy without serious toxic effect.

Double Patenting

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 19-22, 24, 26-28 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 13-19 of copending Application No. 09/987,930. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims found in each application cover very same scope. The claimed subject matter of instant application is directed to a method of treating an affective disorders using an active metabolite of bupropion, their salts, solvates and clathrates thereof whereas the subject matter of the copending application '931 is directed to a method of treating an affective disorders using an active metabolite of bupropion, their salts, solvates, hydrates and clathrates thereof. The scope of the invention of the instant application is very same to the other('930) except the hydrates that additionally required by the instant application('931).

Thus, the claims 19-22, 24, 26-28 are obvious over the claims of the copending application of '930 where the claims in each application are not patentably distinguished from one to another.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

5. No claims is allowed.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vickie Kim whose telephone number is 703-305-1675. The examiner can normally be reached on Tuesday-Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel can be reached on 703-308-4725. The fax phone numbers for the organization where this application or proceeding is assigned are 703-746-3165 for regular communications and 703-746-3165 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Vickie Kim,
Patent examiner
September 17, 2003
Art unit 1614